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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,227	05/18/2005	Igor Yu Galaev	PU0242	2606

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GE HEALTHCARE BIO-SCIENCES CORP.
PATENT DEPARTMENT
800 CENTENNIAL AVENUE
PISCATAWAY, NJ 08855

EXAMINER	
HENRY, MICHAEL C	

ART UNIT	PAPER NUMBER
1623	

MAIL DATE	DELIVERY MODE
06/23/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,227	GALAEV ET AL.	
	Examiner	Art Unit	
	MICHAEL C. HENRY	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-10,12-14 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 6-10, 12-14, 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 03/10/09 affects the application, 10/517,227 as follows:

1. Claims 1, 3, 6, 7, 12, 13, 16 have been amended. Claims 4-5 and 17 have been canceled. The rejections made under 35 U.S.C. 103(a) of the prior office action mailed 12/24/08 are maintained
2. The responsive to applicants' arguments is contained herein below.

Claims 1-3, 6-10, 12-14, 16 are pending in application

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 6-10, 12-14, 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Snoke et al. (US 4,055,469) in view of Izumrudov et al. (Biopolymers (nucleic acid sciences), Vol. 52, 94-108 (1999).

In claim 1, applicant claims a method of isolating a plasmid from a cell lysate which contains other species including nucleic acids, proteins, other high molecular weight compounds, salts and other low-molecular weight substances, which method comprises selectively precipitating the plasmid, while leaving the other species in solution, by adding a polycationic precipitating agent to the solution and allowing it to form an insoluble complex with said plasmid, wherein the precipitating agent is a highly charged linear polymer that includes quaternary amino groups, and further wherein the precipitating agent is added to the solution in

the presence of a salt, wherein the amount of said precipitating agent is sufficient to attain a charge ratio [+] / [-] between the precipitating agent and plasmid of ≥ about 0.5 during the precipitation, further wherein the salt concentration of the solution is controlled during the addition of the precipitating agent to allow quantitative selective precipitation of the plasmid/polycation complex. Claims 2, 8-10 are drawn to the method of claim 1, wherein the precipitating agent includes specific positive charges, specific ratio of polymer molecular wt to polymer charge in the precipitating agent, precipitating agent of specific positive charge, specific precipitating agents including poly(N',N'-dimethyldiallylammonium) chloride, ionene bromide and poly(N-alkyl-4-vinylpyridinium). Claim 3 is drawn to said method further comprising a step of estimating the number of negative charges in the biological solution before addition of the precipitating agent. Claims 6-7 are drawn to said method involving specific biological solutions. Claim 12 is drawn to the method of claim 1, further comprising recovering plasmid (nucleic acid) from the precipitate formed by separating the precipitate from solution and subsequent dissolution and/or destruction of the complex. Claims 13-14 are drawn to said method involving the dissolution or destruction of the polyelectrolyte complex by addition of salt and of salt of specific concentration depending on the charge ratio and salt nature. Claims 16 is drawn to said method comprising first and second isolations of plasmid (nucleic acid) from the biological solution. It should be noted that applicant's claim 1 which recites the phrase "isolating a plasmid from a cell lysate which contains other species including nucleic acids" does not exclude the use of a composition or cell lysate that contains only plasmid DNA(s) as the only nucleic acids and thus the said claim also encompasses the isolation of any plasmid DNA.

Snoke et al. disclose a method of isolating a desired nucleic acid (which includes plasmid) from a biological solution, that may contain other species including proteins, which method comprises selectively precipitating the desired nucleic acid (which includes plasmid), while leaving the other species in solution, by adding a polycationic precipitating agent to the solution and wherein the precipitating agent is a highly charged linear polymer that includes quaternary amino groups, and further wherein the precipitating agent is added to the solution in the presence of a salt (see abstract, example 6 and claims).

The difference between applicant's claimed method and the method taught by Snoke et al. is that Snoke et al. do not disclose the formation of an insoluble complex of the nucleic acid and the precipitating agent nor a need for the amount of precipitating agent to be sufficient to attain a charge ratio [+] / [-] between the precipitating agent and nucleic acid of ≥ about 0.5 during the precipitation.

Izumrudov et al. disclose that polycationic agents or polycationic polymers poly(N',N'-dimethyldiallylammonium) chloride, ionene bromide and poly(N-alkyl-4-vinylpyridinium) bind to DNA (nucleic acid which includes plasmid) and forms a complex and that the stability of the complexes can be controlled by varying e.g. the salt concentration (see page 104, paragraph 3 to page end of page 10). Furthermore, Izumrudov et al. disclose that the addition of salt can dissolve or destruct the complex (see abstract).

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made to have used the method of Snoke et al. to isolate a desired nucleic acid such as a plasmid from a biological solution comprising selectively precipitating the desired nucleic acid, by adding a polycationic precipitating agent to the solution in the presence of salt and in

view of Izumrudov et al. to allow the formation of an insoluble complex of the precipitating agent with said desired nucleic acid and to determine the amount of precipitating agent such as in terms of the charge ratio of precipitating agent to nucleic acid that is required to produce a complex as taught by Izumrudov et al. which can be separated by adjusting the salt concentration.

One having ordinary skill in the art would have been motivated to use the method of Snoke et al. to isolate a desired nucleic acid such as a plasmid from a biological solution comprising selectively precipitating the desired nucleic acid, by adding a polycationic precipitating agent to the solution in the presence of salt and in view of Izumrudov et al. to allow the formation of an insoluble complex of the precipitating agent with said desired nucleic acid and to determine the amount of precipitating agent such as in terms of the charge ratio of precipitating agent to nucleic acid that is required to produce a complex as taught by Izumrudov et al. which can be separated by adjusting the salt concentration. In addition, it should be noted that a substance such as the said complex precipitates from solution when the net charge is zero thus a skilled artisan would be motivated to determine the limiting amount of precipitating agent that is required to form the said complex and to ensure precipitation. Furthermore, it should be noted that it is obvious to repeat the addition of precipitating agent to the remaining biological solution so as to precipitate, obtain or isolate a greater yield or quantity of said nucleic acid. In addition, Izumrudov et al. disclose that the addition of salt can dissolve or destruct the complex (see abstract). Consequently, one of ordinary skill in the art would be motivated based on the teachings of Izumrudov et al. to vary, alter or control the salt concentration such as during the

addition of precipitating agent. In addition, a skilled artisan would be motivated to alter the salt concentration as to optimize the formation and/or stability of the complex precipitated.

Response to Arguments

Applicant's arguments with respect to claim 1-3, 6-10, 12-14, 16 have been considered but are not found convincing, consequently the rejection is maintained.

The applicant argues that Snoke et al. relates to methods for the purification of microbial enzyme extracts, and removing the impurities by precipitation. Although Example 6 discusses that nucleic acids can be precipitated selectively, it does not teach or suggest the differential separation of one type of nucleic acid from a cell lysate including other types of nucleic acids. However, Snoke et al. method does specifically precipitate the desired nucleid acid (which includes plasmid). Snoke et al. states that at high salt concentrations (0.05 M phosphate buffer, pH 7.0), nucleic acids were precipitated selectively (specifically) (see example 6, col. 9). This implies or suggests that a specific nucleic acid (including plasmid) will precipitate at a specific high salt concentration. In addition, it should be noted that the above rejection was made by combining Snoke et al. and Izumrudov et al. wherein Izumrudov et al. disclose that polycationic agents or polycationic polymers poly(N',N'-dimethyldiallylammonium) chloride, ionene bromide and poly(N-alkyl-4-vinylpyridinium) bind to DNA (nucleic acid which includes plasmid) and forms a complex and that the stability of the complexes can be controlled by varying e.g. the salt concentration (see page 104, paragraph 3 to page end of page 10). Furthermore, Izumrudov et al. disclose that the addition of salt can dissolve or destruct the complex (see abstract). Thus, the varying of the salt concentration can further control the stability of the complex or precipitate formed and thus, the nucleic acid (such as plasmid) precipitated or formed.

The applicant argues that Izumrudov et al. relates to nucleic acids in complex with polyamines. However, these are obtained using very pure calf thymus DNA preparations. This is in contrast with the present invention which relates to isolation of plasmid from impure starting material such as a cell lysate. However, Izumrudov et al. disclose that polycationic agents or polycationic polymers poly(N',N'-dimethyldiallylammonium) chloride, ionene bromide and poly(N-alkyl-4-vinylpyridinium) bind to DNA (nucleic acid which include plasmid) and forms a complex and that the stability of the complexes can be controlled by varying e.g. the salt concentration (see page 104, paragraph 3 to page end of page 10). Furthermore, Izumrudov et al. disclose that the addition of salt can dissolve or destruct the complex (see abstract). Consequently, Snoke et al. in view of Izumrudov et al. would be motivated to allow the formation of an insoluble complex of the precipitating agent with said desired nucleic acid and to determine the amount of precipitating agent such as in terms of the charge ratio of precipitating agent to nucleic acid that is required to produce a complex as taught by Izumrudov et al. which can be separated by adjusting the salt concentration (see above rejection. It should be noted that plasmid is alsoDNA. It should also be noted that the above rejection was made by combining Snoke et al. and Izumrudov et al.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 571-272-0652. The examiner can normally be reached on 8.30am-5pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael C. Henry
June 20, 2009.

/Shaojia Anna Jiang/
Supervisory Patent Examiner
Art Unit 1623